# Infringement of patents for new uses of known drugs

## Lessons from recent cases

Van Caenegem, William

*Published in:*
Australian Intellectual Property Law Bulletin

Australian
Intellectual Property Law
Bulletin

# Infringement of patents for new uses of known drugs: lessons from recent cases

***William van Caenegem*** *BOND UNIVERSITY*

## Points to consider

- Patents for new therapeutic uses of known drugs or new dosage regimes are commonly granted in Australia.
- Some recent federal court decisions indicate that such patents might be infringed in multiple ways.
- Infringement can be by doctors prescribing drugs for certain conditions, or by generic drug manufacturers supplying drugs for the purpose of treating those conditions.
- Drug manufacturers may be liable because of the terms of the PDI, or because they had reason to believe that the drug would be prescribed by doctors for a condition covered by the patent.

## Introduction

In Australia, a patent may be granted for a new therapeutic use of a known drug, or for new dosage regimes or administrations of known drugs. This article looks at three recent cases where the Federal Court considered what amounts to infringement of these patents. They are infringed only if the medication is prescribed or supplied for the new therapeutic purpose (a new indication), and not if they are prescribed to treat some other condition.

In a typical situation, infringement of such a process patent for prescription medication can arise in different ways, such as by breach of s 117 of the Patents Act 1990 (Cth) if the pharmaceutical company (often a generic manufacturer) supplies the medication with instructions (a PDI) to prescribe it for the new indication, or having reason to believe that it would be prescribed for the new indication. This is known as infringement by supply.

Alternatively, the supplier may infringe by having authorised the infringing use (s 13 of the Patents Act prescribes that a patent can be infringed by exploitation or by authorising another to exploit it), or as a joint tortfeasor with the prescribing doctor. Also, a doctor who prescribes medication to a patient is held to exploit the patent directly, and thus infringes if not authorised to prescribe it for that particular treatment purpose. This is despite the fact that the doctor neither makes nor directly supplies the medication, nor necessarily knows whether the patient obtains and takes the medication as prescribed. Because such process patents cover a method of prescribing a drug, the actual patient taking the drug, even for an indication covered by the patent, would not infringe.

This article particularly considers s 117 infringement by supply and also infringement by a prescribing doctor, in light of the decisions in:

- *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd (No 2);*[1]
- *Generic Health Pty Ltd v Otsuka Pharmaceutical Co Ltd;* and[2]
- *Apotex Pty Ltd v AstraZeneca AB (No 4).*[3]

## Infringement of process patents for new indications

A process patent, being a patent that covers a practical process or method rather than a product, can be infringed by implementing the method or process without authority (ie, by "exploitation"), or by supplying products to a person for use in a manner covered by the patent (s 117, infringement by supply). Some patents also claim new methods of prescribing drugs (eg, new dosage regimes) for known therapeutic purposes. Such patents are thought to be a significant incentive for pharmaceutical companies to conduct research and development into improved use or hitherto unknown therapeutic benefits of known drugs. Both infringement by exploitation and infringement by supply in such circumstances have recently been considered in a number of Federal Court cases.

In *Apotex v Sanofi-Aventis,* the claim was for a process consisting of the administration of the known substance leflunomide by a medical practitioner for the treatment of psoriasis. The substance was previously known and used for the treatment of arthritic conditions. The application of leflunomide in accordance with the patent thus necessarily involved diagnosis of psoriasis by a medical practitioner and prescription of the drug for its treatment.

Thus, a medical practitioner who prescribes leflunomide for arthritis would not infringe the relevant patent, but one who prescribes it for psoriasis (a skin condition)

would infringe the patent if not authorised by the patentee to do so. Importantly, the medical practitioner would be a primary infringer in those circumstances, guilty of exploiting the patent without authority, rather than an infringer by supply under s 117 of the Patents Act. In practice, whether or not the patent is infringed would largely depend on who prescribes it: therefore, a dermatologist prescribing leflunomide would infringe the patent, whereas most likely a rheumatologist who does so would not.

The additional complication in this case was that psoriasis and the rheumatic condition PsA often present together in a patient. However, according to the Full Court, a rheumatologist who prescribes leflunomide for a rheumatic condition, where the drug would also ameliorate psoriasis, would not infringe the patent because of the fact alone that the administration also had a clinically beneficial result relating to psoriasis (in this the Full Court overturned the trial judge's decision).

Section 117 of the Patents Act (infringement by supply) specifies that a person may infringe the patent not by applying the process covered by the claims, but by supplying products to a party who will put them to use in the claimed manner (method or process). In this context, the company supplying the drug rather than the doctor prescribing it might infringe by supply. But liability will only ensue if one of a number of conditions is fulfilled: if the product is only capable of a use that is patented (s 117(2)(a)); if the product supplied is not a staple commercial product, and it is put to an infringing use, as long as the supplier had reason to believe that the recipient would put it to that use (s 117(2)(b)); and where there is an infringing use that accords with instructions or inducements supplied with the product or contained in an advertisement published by or with the authority of the supplier (s 117(2)(c)).

In terms of a process patent for the use of a known compound for a new clinical indication, such as in the *Sanofi-Aventis* case, the supplier's (the pharmaceutical company's) liability for infringement by supply will most often result from instructions or product information (PID) contained within or on the packaging of the drug. In *Sanofi-Aventis*, the facts indicated that psoriasis often occurs at the same time as the particular rheumatic condition (PsA) in a particular patient. In the result, the court held that:

> The appellant's PID instructed the use of leflunomide in the treatment of psoriasis which is associated with PsA, as will commonly be the case. On that basis, s 117(2)(c) is engaged.[4]

Further, Keane J held that the contents of the instructions in the PID also made it apparent that the appellant (Apotex) also had "reason to believe" (s 117(2)(b)) that "medical practitioners would put leflunomide to use as a method of treating psoriasis which is associated with PsA".[5] The court concluded that s 117 would therefore be engaged on two grounds: because of the *specific instruction* in the PID referred to above; and because the appellant had *reason to believe* that the product would be prescribed in certain cases to treat concurrent psoriasis. The reasonable belief could be inferred from the content of the PID.

## What amounts to reasonable belief?

The latter point relating to "reasonable belief" in s 117(2)(b) is particularly relevant in light of the further case of *Generic Health Pty Ltd v Otsuka Pharmaceutical Co Ltd.*

The claim related to a method of administering to patients a therapeutically effective amount of the known drug aripiprazole for the treatment of cognitive impairment in patients suffering from treatment-resistant, inveterate or chronic schizophrenia who failed to respond to two or more of a list of anti-psychotic drugs specified in the patent claims.

Cognitive impairment is typically treated by atypical anti-psychotic drugs, but some patients are resistant to such therapy and, in these cases, the administration of aripiprazole may be a potent therapy. Here the "reasonable belief" could not be implied from the PID as in the *Sanofi-Aventis* case above. Rather, the reasonable belief was only based on evidence of a more general kind, it being established law that no actual belief need be shown and the section providing that the belief must be that the product *would* (not might) be used in an infringing manner.

In that context, the court stressed that facts were in evidence that gave rise to a reasonable belief that aripiprazole was prescribed by doctors to treat the cognitive impairment schizophrenia sufferers are known to experience:

> The medical evidence addresses the use of aripiprazole in the treatment of schizophrenia-associated cognitive impairment and the basis of such action. There is evidence that patients may be "switched" to aripiprazole. This was not a case of possible hypothetical infringing use. The evidence established, at a prima facie level, that there was reason to believe on the part of the supplier, a supplier of pharmaceutical products, that it would be put to the claimed use.[6]

Thus, the evidence that resulted in liability in this case is much more general in nature than in the *Sanofi-Aventis* case. It should be noted that the consideration of the Full Court was in the context of an appeal against an interlocutory injunction.

## Apotex v AstraZeneca

In *Apotex v AstraZeneca*, the patent related to the use of rosuvastatin in particular dosages. AstraZeneca (AZ) relied on s 117 of the Patents Act, but also on joint

tortfeasorship to the extent that "by the act of supply, [Apotex et al] would be aiding, inducing or procuring the infringement of the patent by patients who used the products in issue".[7] Interestingly enough, AZ also submitted that s 13(1) would be infringed because it provides that "Subject to this Act, a patent gives the patentee the exclusive rights, during the term of the patent, to exploit the invention *and to authorise* another person to exploit the invention", and that such authorisation had occurred here.

Thus, apart from infringement by exploitation by the doctor prescribing a drug for a patented indication, and infringement by supply based on s 117, the decision suggests that two further forms of infringement may arise in these types of supply and process patent cases. This is important for practitioners to keep in mind. However, here the question of infringement was hypothetical, as the court found the patent to be invalid on a number of grounds. Nonetheless, it went on to consider the question of liability obiter.

The court took issue with Keane J's approach in *Sanofi-Aventis*.[8] But a question issue arose, in that the patent in this case was for the administration of a particularly low dose of the known substance, which was surprisingly effective in the treatment of extreme hypertension. Some of the evidence indicated the availability in pharmacies of pill-splitters, machines that enable a pill to be cut into smaller parts, thus enabling the administration of doses smaller than a whole pill. A generic equivalent pill supplied in a dose that itself would not be infringing because not falling within the low-dose patent might in those circumstances become an infringing supply. That would be the case if the PID instructed the use of a pill-splitting device, and so on, but also if the supplier had *reason to believe* that a purchaser would split the pills into the lower dosages falling within the claims.

The court stressed that AZ ultimately had to prove that a person would use the 40 mg product supplied by Apotex within the claims of the low dose (5 and 10 mg) patent, and went on to say that it was ultimately satisfied:

> Given the ease of tablet splitting by using a pill cutter, whether the tablet be scored or unscored, and the economic incentives, that there is a risk that some people will obtain the 20 mg dose of the generic tablets for the purpose of dividing them into two 10 mg doses. I also infer that this risk will exist irrespective of any instructions the generic parties might send to medical practitioners and pharmacists not to endorse tablet splitting in any way because, ultimately, *the obligation of medical practitioners and pharmacists is to their patients and not to drug companies who want to try to avoid patent infringements.* The risk also remains despite Apotex's product information directing against tablet splitting. [Emphasis added.][9]

The court concluded in relation to s 117(2)(c) that:

> … on the whole of the evidence, including the proposed communications with medical practitioners and pharmacists, it cannot be said that the generic parties will instruct or induce any person to split a 20 or 40 mg tablet into two or four.[10]

Despite this conclusion, the comments the court makes in relation to the risk of pill splitting have potentially far-reaching implications. Even if PID instructions counsel against the pill splitting practice, it *may be* that because medical practitioners would instruct patients to split pills, taken together with other evidence, the generic supplier would be held to have had a "reasonable belief" that the product would be prescribed in a manner that would infringe the process patent. It should be noted that the court held that the pharmaceutical substance was not a staple commercial product: although it had various uses in relation to hypertension, its uses did not stretch to treatment of other conditions.

## Points from these cases…

These cases thus illustrate a number of points. First, there is a considerable list of potential heads of liability where a generic manufacturer supplies medication that is prescribed for the treatment of a condition as covered by a process patent:

- prescription of the drug to a patient by the doctor can amount to primary infringement by exploitation;
- supply of a drug to a doctor with instructions to use it for treatment of a particular medical indication that is covered by a method patent may amount to infringement by supply (s 117);
- supply of a drug where there is reason for the supplier to believe, from general evidence about medical knowledge and practice, that it will, at least in part, be prescribed for a condition covered by a method patent may amount to infringement by supply (s 117);
- infringement by authorisation may occur where a drug is supplied with instructions to use it in a manner covered by a process patent (primary infringement (s 13(1)); and
- liability as a joint tortfeasor with the prescribing doctor where supplying a drug for an infringing use is also a possibility.

The latter two points have not been further considered here, but should be kept in mind.

This means that suppliers of generic drugs that have non-patented and patented uses have to tread very carefully in terms of the content of their PIDs. If the obiter statements in the *AstraZeneca* case are to be given

any credit, then it may be that in some circumstances, no matter how carefully drafted the PID is, the supplier of a generic drug may still be at risk of liability because the widespread knowledge about the use of a drug for a certain condition or in a certain manner means that the conclusion that the supplier had a "reasonable belief" that it would be put to an infringing use is inescapable.

## Medical treatment patents for secondary indications

On a final point, an issue that recurs in relation to medical treatment method patents for new uses of known therapeutic substances is whether such "inventions" actually disclose patentable subject matter. However, the acceptance of patentability of such secondary indications is now firmly anchored in Australian patent case law. The courts refuse to tamper with the present law, preferring to leave this to parliament. However, as we know, the parliament in 1990, by retaining the "manner of manufacture" terminology in s 18 of the Patents Act, has left the matter firmly in the judges' court. The manner of manufacture question has also arisen in the context of the *Philips*[11] threshold test of invention but, there too, opponents of medical treatment patents have received little comfort from the courts.

***Professor William van Caenegem***
*Faculty of Law*
*Bond University*
*wvancaen@bond.edu.au*

## Footnotes

1. *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd (No 2)* (2012) 204 FCR 494; 290 ALR 1; [2012] FCAFC 102; BC201205205.
2. *Generic Health Pty Ltd v Otsuka Pharmaceutical Co Ltd* (2013) 296 ALR 50; [2013] FCAFC 17; BC201300958.
3. *Apotex Pty Ltd v AstraZeneca AB (No 4)* [2013] FCA 162; BC201300937.
4. Above, n 1, at [54] per Keane CJ as he then was.
5. Above, n 1, at [54].
6. Above, n 2, at [108] per Bennett J.
7. Above, n 3, at [486].
8. Above, n 3, at [505]–[508].
9. Above, n 3, at [508].
10. Above, n 3, at [510].
11. *NV Philips Gloeilampenfabrieken v Mirabella International Pty Ltd* (1995) 183 CLR 655; 132 ALR 117; 32 IPR 449; BC9501525.